

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference NP 0015	FOR FURTHER ACTION see Form PCT/ISA/220 as well as, where applicable, item 5 below.	
International application No. PCT/EP2004/013683	International filing date (day/month/year) 01/12/2004	(Earliest) Priority Date (day/month/year) 02/12/2003
Applicant NICOX S.A.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 5 sheets.

It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**

a. With regard to the language, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

The international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, see Box No. I.

2. Certain claims were found unsearchable (See Box II).

3. Unity of invention is lacking (see Box III).

4. With regard to the title,

the text is approved as submitted by the applicant.

the text has been established by this Authority to read as follows:

NITROOXYDERIVATIVES OF CARVEDILOL AND OTHER BETA BLOCKERS AS ANTIHYPERTENSIVE DRUGS

5. With regard to the abstract,

the text is approved as submitted by the applicant.

the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. With regard to the drawings,

a. the figure of the drawings to be published with the abstract is Figure No. _____

as suggested by the applicant.

as selected by this Authority, because the applicant failed to suggest a figure.

as selected by this Authority, because this figure better characterizes the invention.

b. none of the figures is to be published with the abstract.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/EP2004/013683

Box No. IV Text of the abstract (Continuation of item 5 of the first sheet)

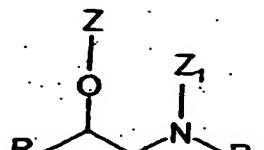
The present invention relates to β -adrenergic blockers nitrooxyderivatives of general formula (I):



wherein

s is an integer equal to 1 or 2;

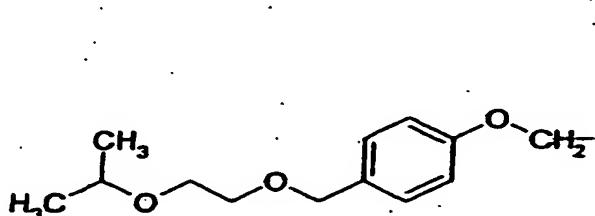
A is selected from the following β -adrenergic blockers residues of formula (II):



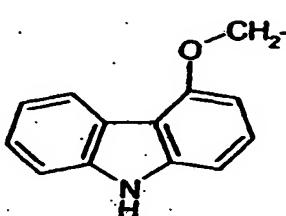
101

wherein

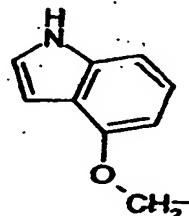
R₁ is selected from the group consisting of:



(IIa)



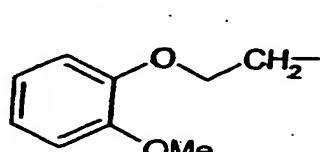
(1b)



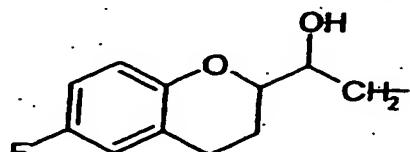
(11c)

or other residues defined in claim 1;

R_2 is selected from the group consisting of: $-\text{CH}(\text{CH}_3)_2$, $-\text{C}(\text{CH}_3)_3$ or



(IIIa)



(11b)

Z is H or is a group capable of binding Y as defined in claim 1

Z_1 is H or a $-C(O)-$ capable of binding Y.

the other substituents are defined in claim 1;

and enantiomers and diastereoisomers and pharmaceutically acceptable salts thereof, pharmaceutical compositions containing them and their use for the treatment of hypertension, cardiovascular diseases, glaucoma, migraine headache and vascular diseases.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP2004/013683

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K31/403 C07D209/88 C07C203/04 A61P9/12

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K C07D C07C A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 98/21193 A (NICOX) 22 May 1998 (1998-05-22) cited in the application the whole document -----	1-98
A	EP 0 637 583 A (PRODESFARMA) 8 February 1995 (1995-02-08) cited in the application the whole document -----	1-98
A	EP 0 200 915 A (BOEHRINGER MANNHEIM) 12 November 1986 (1986-11-12) the whole document ----- -/-	1-98

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

° Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *&* document member of the same patent family

Date of the actual completion of the international search

17 March 2005

Date of mailing of the international search report

31/03/2005

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP2004/013683

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	JAYACHANDRAN ET AL: "Up-regulation of endothelial nitric oxide synthase through beta2-adrenergic receptor: The role of a beta-blocker with NO-releasing action" BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, vol. 280, no. 3, 2001, pages 589-594, XP002321567 the whole document -----	1-98

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No	
PCT/EP2004/013683	

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9821193	A 22-05-1998	IT MI962368 A1 AT 226199 T AU 729423 B2 AU 5551998 A BR 9712959 A CA 2272063 A1 CN 1242768 A ,C DE 69716461 D1 DE 69716461 T2 DK 941218 T3 WO 9821193 A1 EP 0941218 A1 ES 2186013 T3 HU 0000667 A2 IL 129768 A JP 2001507676 T KR 2000053251 A PT 941218 T RU 2190594 C2 SI 941218 T1 US 6242432 B1	14-05-1998 15-11-2002 01-02-2001 03-06-1998 01-02-2000 22-05-1998 26-01-2000 21-11-2002 26-06-2003 17-02-2003 22-05-1998 15-09-1999 01-05-2003 28-07-2000 19-02-2004 12-06-2001 25-08-2000 31-03-2003 10-10-2002 28-02-2003 05-06-2001
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